ORIGINAL ARTICLE

Should malnutrition risk be assessed in older patients with elevated levels of NT-proBNP?

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KEY WORDS

densitometry, elderly, heart failure, malnutrition risk, NT-proBNP

ABSTRACT

INTRODUCTION An inverse relationship between natriuretic peptides (N-terminal fragment of the prohormone brain natriuretic peptide [NT-proBNP]) and body mass index (BMI) among healthy people and patients with chronic heart failure (CHF) was observed.

OBJECTIVES The aim of the study was to assess the relationship between nutritional status and NT-proBNP concentrations in older persons.

PATIENTS AND METHODS NT-proBNP concentrations, medical histories, and malnutrition risk using Mini Nutritional Assessment were evaluated. Body composition was measured with dual energy X-ray absorptiometry. The relationship of nutritional status with NT-proBNP concentrations (in tertiles) was assessed.

RESULTS The mean (SD) age of 106 participants was 72.16 (9.38) years. Heart failure was diagnosed in 72.6% of patients. The risk of malnutrition was recognized in 28.3%, and the percentage of patients at risk increased in subsequent NT-proBNP tertiles: from 16.7% in the first tertile to 48.6% in the third tertile ($P = 0.005$). The risk of malnutrition was associated with an increase in NT-proBNP concentrations per tertile (odds ratio [OR], 2.30; 95% CI, 1.30–4.07; $P = 0.004$). Based on a multivariable logistic model, the NT-proBNP concentration in the third tertile was associated with an over 9-fold higher risk of malnutrition (OR, 9.80; 95% CI, 2.00–48.17; $P = 0.005$) as compared with the lowest concentration. Among patients with CHF, the relationship between NT-proBNP and nutritional status was even stronger.

CONCLUSIONS High NT-proBNP levels contribute to increased risk of malnutrition in older patients with heart failure. In patients with elevated NT-proBNP levels, the risk of malnutrition should be assessed.

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INTRODUCTION The problem of malnutrition, a risk factor for increased morbidity and reduced quality of life, is often underestimated in the geriatric population.[1,2] In general, the term "malnutrition" refers to an improper balance in catabolic and anabolic metabolism reactions and to protein–energy malnutrition.[3] According to the recent guidelines of the European Society of Clinical Nutrition and Metabolism, the term should be treated as a synonym for undernutrition.[4] It may be a result of long-lasting chronic conditions, especially in advanced age, and in patients with multiple chronic conditions. One of the diseases often accompanied by malnutrition is heart failure (HF). Advanced HF is often associated with severe muscle wasting, called cardiac cachexia, which consequently affects the disease course and significantly decreases the quality of life and survival in patients with HF.[5] In everyday practice, nutritional status is assessed by means of the body mass index (BMI); however, BMI does not distinguish between fat and lean body mass. In HF, even patients without cardiac decompensation have excess fluid compared with a standard healthy individual[6]; therefore, some patients who are regarded as having normal body weight may, in fact, be

underweight. It is important to identify patients who are at risk because malnutrition is largely irreversible, especially in the elderly. In the latest research,[7] it was shown that all-cause mortality was minimal in a BMI range of 20.0 to 25.0 kg/m^2, and it was significantly increased just below this range. In older age groups, the lowest mortality was found at a slightly higher BMI than in younger age groups. Moreover, in patients with acute or stable HF, a higher BMI was strongly associated with decreased mortality.[8,9] This phenomenon is called "reverse epidemiology" or "obesity paradox".[10,11]

Several published studies have documented an inverse relationship between BMI and markers of HF, including brain natriuretic peptides (BNPs) and N-terminal fragment of the prohormone BNP (NT-proBNP)[12-14]; these markers are used to assess the presence and severity of HF. The inverse relationship was observed among healthy people, patients with an acute chronic HF (CHF) exacerbation, and patients with stable, well-controlled CHF.[15,16] Obese patients have reduced concentrations of BNP and NT-proBNP, compared with non-obese ones, despite having elevated left ventricular end-diastolic pressure.[17] Although BNP and NT-proBNP levels are relatively lower in overweight and obese patients with HF, increased concentrations predict worse symptoms, impaired hemodynamics, and higher mortality at all BMI levels.[18]

Thus far, the relationship between BNP levels and malnutrition–inflammation syndrome was mainly assessed in patients with end-stage renal disease. In this chronic condition, the association of elevated BNP levels with left ventricular hypertrophy and increased risk of death has been extensively studied.[19,20] Recently, Di Marca et al[21] showed that increased BNP levels, along with malnutrition and chronic kidney disease, predict 30-day mortality after discharge in elderly patients with diagnosis on admission other than HF. Especially in the hemodialysis population, natriuretic peptides are considered to be potential malnutrition biomarkers.[18,22-28] Moreover, in patients with systemic sclerosis,[29] high NT-proBNP levels were associated with reduced nutritional status. To our knowledge, only one study assessed nutritional status using the Mini Nutritional Assessment (MNA) screening score and found a significant inverse correlation between the score and NT-proBNP levels in patients with systolic HF.[30]

We aimed to further explore the association between NT-proBNP levels and nutritional status in elderly patients with multiple chronic conditions. We also examined the relationship between NT-proBNP levels and risk of malnutrition in this population.

PATIENTS AND METHODS

Study design and patient enrollment

The study had a cross-sectional design. Patients aged 60 years or older followed in the Geriatric Outpatient Clinic of the University Hospital in Kraków, Poland, who agreed to participate in the study and signed informed consent, were included from October 2010 to February 2014.

The exclusion criteria were as follows: Mini Mental State Examination (MMSE) score below 10 and immobility. If the patient had cognitive impairment or dementia, the interview was completed by a proxy.

In all patients, demographic data, smoking status, and medical history of chronic conditions and medications were obtained using a structured questionnaire. The obtained data was supplemented in accordance with the medical documentation. Height (m) and weight (kg) were measured and BMI (kg/m^2) was calculated according to the formula: weight (kg)/height (m^2).

The risk of malnutrition was assessed using the MNA with a maximal score of 30 points and a score of 24 or higher suggesting normal nutritional status; scores between 17 and 23.5 indicated a risk of malnutrition, and below 17, malnutrition.[31] Due to a low number of malnourished persons with an MNA score of less than 17 in the analysis, we combined the group of individuals with the score of less than 17 with those at risk of malnutrition (17–23.5 points); therefore, the MNA score of less than 24 was used as the categorical variable.

Cognitive performance was evaluated using the MMSE, in which a score below 24 of 30 suggests cognitive impairment.[32] Mood was assessed with the 30-point Geriatric Depression Scale (GDS), in which a score above 9 points gives a suspicion of depression.[33]

Functional status was assessed by the Instrumental Activities of Daily Living (IADL) scale, with a maximum score of 27 points and the assumption that the higher the score the better the functional status.[34] The Katz Index of Activities of Daily Living was also used for functional status assessment, with the score ranging from 0 to 6 and interpreted as follows: 5 to 6 points, people efficient in basic self-service; 3 to 4 points, moderately disabled; and 0 to 2 points, severely disabled.[35]

Chronic kidney disease was defined as an estimated glomerular filtration rate (eGFR) below 60 ml/min/1.73 m^2, according to the Modification of Diet in Renal Disease formula.

Left ventricular ejection fraction was measured by transthoracic echocardiography (Toshiba Xario XG, Japan) with a 2.5- to 3.5-MHz probe.

The body composition including total lean body mass, appendicular lean mass, and body fat (total, trunk, and appendicular body fat) was examined using dual energy X-ray absorptiometry (Lunar Prodigy, General Electric Medical Systems Madison Wisconsin, United States).

A serum NT-proBNP level was measured by an electrochemiluminescence immunoassay method (NT-proBNP, Roche Diagnostics GmbH, Germany, Mannheim) with a Roche immunoassay analyzer.

The study was approved by the Bioethical Committee of Jagiellonian University (Kraków, Poland). All subjects signed an informed consent to participate in the study.

Statistical analysis Statistical analysis was carried out using Stata/SE 14 (Stata Corp, College Station, Texas, United States). The results were presented as mean (SD) or as frequency and percentages for nominal variables. Patients were divided into 3 groups according to the tertiles of plasma NT-proBNP concentrations. The mean values for continuous variables in these groups were compared using 1-way analysis of variance and percentages for nominal variables using the χ^2 test. In addition, to assess the association between NT-proBNP levels and continuous predictors, the Spearman correlation was used.

The impact of selected predictors on the risk of malnutrition was analyzed by logistic regression models. First, the univariate logistic regression models were built to assess the crude (unstandardized) odds ratios (ORs) for the relationship between the studied variable and the risk of malnutrition. Next, in the multivariable logistic regression model, the effect of the MMSE score (as a significant predictor in the univariate model) and a set of confounders based on literature (ie, chronic kidney disease, age, functional status [IADL], CHF, and a number of chronic diseases) on the relationship between NT-proBNP tertiles and malnutrition was assessed. Additionally, we analyzed the effect of NT-proBNP on malnutrition risk using a model with NT-proBNP as a continuous variable (expressed per 100 pg/ml). An additional analysis was performed to assess the relationship between NT-proBNP levels and malnutrition risk in the group of patients with HF. The results were adjusted for the same set of independent variables as in the whole group. In all statistical analyses, 2-sided tests were used. *P* values of less than 0.05 were considered significant.

RESULTS The mean (SD) age of 106 individuals (men, 58.5%) was 72.16 (9.38) years. The mean (SD) number of chronic conditions was 5.6 (2.5) and the mean (SD) number of medications was 7.15 (2.5). The mean (SD) IADL and ADL scores in the whole study group were 23.65 (3.60) and 5.90 (0.45), respectively. CHF was diagnosed in 77 patients (72.64%). Most of them (57.14%) were in New York Heart Association class III, while 33.77% were in class II. Most patients received standard therapy with an angiotensin-converting enzyme inhibitor (or sartan), diuretic, and β-blocker. No patient presented with overt symptoms of HF during the study.

In the whole group, a negative correlation between the MNA score and NT-proBNP levels was found ($r = -0.23$; $P = 0.02$). Due to its skewed distribution, NT-proBNP concentrations were divided into tertiles; the relationship between NT-proBNP ranges within each tertile and MNA scores were further assessed. The baseline characteristics of the study population, stratified by tertiles of NT-proBNP concentrations, are presented in TABLE 1.

The groups did not differ in terms of age, smoking status, amount of lean body mass; MNA, MMSE, and GDS results; or history of myocardial infarction, stroke, and diabetes mellitus. Higher NT-proBNP levels were correlated with an increased number of patients diagnosed with CHF, coronary heart disease (CHD), and hypertension; in contrast, there was a decreased percentage of female participants. The risk of malnutrition was observed in 30 patients (28.3%) (women, 54.6%; men, 25%). In subsequent NT-proBNP tertiles, higher NT-proBNP levels were associated with an increased likelihood of being malnourished.

BMI and total body fat decreased with an increasing NT-proBNP level (per tertile) ($P = 0.02$ and $P < 0.001$, respectively). Negative correlations between NT-proBNP levels and BMI ($r = -0.19$; $P = 0.048$), body fat amount ($r = -0.33$; $P = 0.005$), and body fat percentage ($r = -0.33$; $P = 0.049$) were found. There was no correlation between NT-proBNP levels and lean body mass.

In a logistic regression analysis, the risk of malnutrition (MNA <24) was introduced as a dependent variable; the impact of potential predictors was assessed in crude (univariate) models (TABLE 2). The concomitant diseases (including hypertension [OR, 0.51; 95% CI, 0.15–1.74], CHD [OR, 0.88; 95% CI, 0.32–2.41], diabetes [OR, 1.25; 95% CI, 0.52–3.04], and CHF [OR, 1.74; 95% CI, 0.63–4.81]) were not associated with the risk of malnutrition.

The risk of malnutrition, defined as an MNA score of less than 24, was over 4-fold higher in patients in the third tertile of NT-proBNP levels in comparison with those in the first tertile (TABLE 2). The trend was significant in the analysis of the entire group. In the crude analysis, an increase in NT-proBNP concentrations (per tertile) was associated with an over 2-fold increase in the risk of malnutrition (OR, 2.30; 95% CI, 1.30–4.07; $P = 0.004$).

With an increase of the NT-proBNP level by 100 pg/ml, the risk of malnutrition increased by 2% (OR, 1.02; 95% CI, 1.01–1.04; $P = 0.009$).

Further analysis, with adjustment for other confounders (age, IADL, MMSE, number of chronic diseases, chronic kidney disease, and HF), confirmed the relationship between the tertiles of NT-proBNP levels and risk of malnutrition. This analysis also revealed the protective role of better cognitive performance, represented by a higher MMSE score (TABLE 3).

A separate analysis for patients with HF (n = 76) and those without (n = 29) was also performed. The relationship (adjusted for age, chronic kidney disease, IADL, MMSE, number of chronic diseases) remained significant only in the HF group. In comparison with patients in the first tertile of NT-proBNP concentrations, the risk of malnutrition was much higher (OR, 26.2; 95% CI, 2.12–324.28) in patients in the third tertile (TABLE 4).

TABLE 1 Characteristics of the study group stratified by tertiles of N-terminal fragment of the prohormone brain natriuretic peptide concentrations

Variable	Tertiles of NT-proBNP level, pg/ml			*P* value
	1st (n = 36) <268.4	2nd (n = 35) 268.4–1339.0	3rd (n = 35) >1339.0	
Age, y, mean (SD)	71.3 (7.6)	73.9 (9.98)	71.3 (10.39)	0.43[a]
Sex, women, n (%)	22 (61.1)	16 (45.7)	6 (17.1)	0.001[b]
Smoking, n (%)	3 (8.6)	4 (11.4)	6 (17.1)	0.54[b]
CHF, n (%)	13 (36.1)	29 (82.9)	35 (100.0)	<0.001[b]
CHD, n (%)	21 (58.3)	31 (88.6)	31 (88.6)	0.002[b]
Arterial hypertension, n (%)	28 (77.8)	32 (91.4)	34 (97.1)	0.03[b]
Myocardial infarction, n (%)	12 (33.3)	16 (45.7)	20 (57.1)	0.13[b]
Stroke, n (%)	4 (11.1)	2 (5.7)	3 (8.6)	0.72[b]
Diabetes, n (%)	11 (30.6)	12 (34.3)	12 (34.3)	0.93[b]
MNA, points, mean (SD)	25.7 (2.72)	25.4 (2.65)	24.4 (2.73)	0.10[a]
BMI, kg/m^2, mean (SD)	29.6 (4.65)	27.8 (4.43)	26.7 (3.81)	0.02[a]
Chronic kidney disease, n (%)	5 (13.9)	9 (25.7)	11 (32.4)	0.18[b]
MNA score <24, n (%)	6 (16.7)	7 (20.0)	17 (48.6)	0.005[b]
MMSE, points, mean (SD)	26.9 (2.81)	26.6 (3.82)	27.0 (2.93)	0.85[a]
GDS, points, mean (SD)	9.7 (6.44)	9.6 (5.84)	9.4 (5.13)	0.98[a]
IADL, points, mean (SD)	23.8 (3.61)	24.3 (3.04)	22.9 (4.06)	0.27[a]
ADL, points, mean (SD)	5.8 (0.71)	5.9 (0.24)	6.0 (0.19)	0.29[a]
Creatinine, µmol/l, mean (SD)	76.2 (21.98)	90.5 (29.61)	104.6 (36.27)	<0.001[a]
Appendicular lean mass, kg, mean (SD)	20.4 (4.26)	19.3 (3.48)	21.5 (4.06)	0.10[a]
Lean body mass, kg, mean (SD)	47.6 (8.97)	46.0 (6.88)	50.2 (8.35)	0.13[a]
Total fat, kg, mean (SD)	41.0 (6.20)	34.6 (7.98)	31.1 (8.22)	<0.001[a]

a Analysis of variance; **b** χ^2 test

Abbreviations: ADL, Activities of Daily Living; BMI, body mass index; CHD, coronary heart disease; CHF, chronic heart failure; GDS, Geriatric Depression Scale; IADL, Instrumental Activities of Daily Living; MMSE, Mini Mental State Examination; MNA, Mini Nutritional Assessment; NT-proBNP, N-terminal fragment of the prohormone brain natriuretic peptide

DISCUSSION The main finding of our study, apart from the inverse relationship between NT-proBNP concentrations and MNA score, was the degree of malnutrition risk associated with increasing NT-proBNP levels. There was an over 2-fold higher risk of malnutrition with an increase of NT-proBNP levels per tertile and an over 9-fold higher risk in patients with the highest NT-proBNP level. Furthermore, in patients with CHF, the higher NT-proBNP level was associated with a 26-fold higher risk of malnutrition for those in the third tertile (after controlling for different confounders).

Additionally, there were negative correlations between NT-proBNP levels and BMI, body fat amount, and body fat percentage; however, there were no correlations between NT-proBNP levels and lean body mass.

Our study examining patients with HF demonstrated a significant relationship between NT-proBNP levels and the risk of malnutrition, an association that was also found in studies examining other groups, also patients without HF. The observation of an inverse relationship between nutritional status and BNPs mainly come from studies in patients with end-stage renal disease.[18,22-28] Other studies examining chronic diseases such as systemic sclerosis[29] and HF,[14,30,36,37] as well as population-based studies,[13,38] were also conducted. The finding concerning the inverse relationship between BMI and NT-proBNP levels remains in line with the results of other authors.[13-17,22,25,30,38-41]

In contrast to the previous research,[13,14] however, our study shows an inverse association between NT-proBNP and fat mass (not lean mass). In comparison with younger populations in some previous studies,[13,14,42] our study population was older with a mean (SD) age of 72.16 (9.38) years. We should consider frequent multimorbidity and chronic inflammatory diseases in our patients, which might influence and intensify different physiologic age-related changes. A negative correlation between NT-proBNP and fat mass was also shown by Christensen et al,[37] although in their prospective study fat mass increased during follow-up. This phenomenon may be related to the lipolytic role of natriuretic peptides through activation of the hormone sensitive lipase,[43] as well as to an increase in energy utilization and thermogenesis by enhancing browning of white adipocytes.[44]

TABLE 2 Crude odds of malnutrition (Mini Nutritional Assessment score <24)[a]

Variable		OR	95% CI	*P* value
NT-proBNP, tertiles	1st	1.00	Ref.	–
	2nd	1.25	0.37–4.17	0.72
	3rd	4.72	1.57–14.17	0.006
Age, y		1.01	0.97–1.06	0.58
Sex (women vs men)		1.62	0.69–3.80	0.27
Smoking (yes vs no)		0.72	0.18–2.83	0.64
CHF (yes vs no)		1.74	0.63–4.81	0.29
CHD (yes vs no)		0.88	0.32–2.41	0.80
Arterial hypertension (yes vs no)		0.51	0.15–1.74	0.28
Myocardial infarction (yes vs no)		1.30	0.56–3.04	0.54
Stroke (yes vs no)		1.30	0.30–5.56	0.73
Diabetes (yes vs no)		1.25	0.52–3.04	0.62
BMI, kg/m^2		0.86	0.77–0.97	0.01
Chronic kidney disease (yes vs no)		1.24	0.47–3.28	0.66
MMSE, points		0.84	0.73–0.97	0.02
GDS, points		1.05	0.98–1.13	0.20
IADL, points		0.90	0.80–1.01	0.08
ADL, points		1.32	0.40–4.41	0.65
Creatinine, µmol/l		1.005	0.99–1.02	0.49
Appendicular lean mass, kg		0.96	0.85–1.07	0.45
Lean body mass, kg		0.97	0.92–1.03	0.36
Total fat, kg		0.98	0.92–1.04	0.51

a Based on the univariate logistic regression model

Abbreviations: OR, odds ratio; others, see TABLE 1

TABLE 3 Logistic regression model for the risk of malnutrition (Mini Nutritional Assessment score <24) (n = 105)

Characteristics		OR	95% CI	*P* value
NT-proBNP	1st	1.00	Ref.	–
	2nd	1.70	0.39–7.52	0.48
	3rd	9.80	2.00–48.17	0.005
Age		1.00	0.95–1.06	0.88
Chronic kidney disease (yes vs no)		1.18	0.35–3.91	0.79
IADL		0.96	0.84–1.10	0.57
MMSE		0.82	0.70–0.97	0.02
No. of diseases[a]		1.17	0.75–1.83	0.50
CHF (yes vs no)		0.29	0.05–1.85	0.19

a Chronic heart failure, coronary heart disease, myocardial infraction, stroke, valvular heart disease, diabetes, arthritis

Abbreviations: see TABLES 1 and 2

On the other hand, lower concentrations of both BNP and NT-proBNP among patients with a higher BMI might be due to reduced synthesis or secretion of peptides, rather than an increased clearance. The results of a recently published study suggest that BNP may be involved in appetite regulation.[45] Vila et al[45] revealed that an intravenous administration of BNP reduces circulating ghrelin concentrations, decreases hunger, and increases the feeling of satiety in healthy people. This may support the existence of a heart–gut–brain axis, which might play a central role in adapting appetite and energy homeostasis to the degree of heart dysfunction. Despite this, age-adjusted NT-proBNP cutoffs to "rule in" HF and age-independent cutoffs to "rule out" HF in patients with acute dyspnea are equally useful for obese and lean patients; an adjustment of NT-proBNP thresholds for BMI is not recommended.[40] The NT-proBNP concentration retains its diagnostic and prognostic capacity across all BMI categories.[25]

The inverse correlation between NT-proBNP and BMI was also shown in individuals without CHF. Fragopoulou et al[38] demonstrated, in their ATTICA study, that NT-proBNP values were positively correlated with age and inversely with BMI, creatinine clearance, and hemoglobin values in an apparently healthy Greek population. A linear regression analysis revealed that sex was the main contributor of NT-proBNP levels, followed by age, BMI, and creatinine levels.

The problem of the association between NT-proBNP and malnutrition was mainly derived from research on patients with end-stage renal disease on hemodialysis. Lee et al[25] concluded that malnutrition in hemodialysis patients is associated with volume overload and increased log-transformed NT-proBNP levels independent of volume status, and these levels are further independently associated with an increased left ventricular mass index. This also suggests a possibility that nutritional status may affect ventricular remodeling in hemodialysis patients.[25] Another example is a study by Guo et al.[24] They demonstrated the association between NT-proBNP and protein-energy wasting adjusted for age, dialysis vintage, and inflammation (OR, 2.3; P = 0.008), which may partly explain the strong relationship between NT-proBNP and mortality in hemodialyzed patients.[24] In the study conducted by Bednarek-Skublewska et al,[23] NT-proBNP levels were elevated in patients with an intensive catabolism, severe anemia, higher mean arterial blood pressure, and longer duration of hemodialysis. Booth et al[22] showed that NT-proBNP was not associated with cardiac dysfunction, as assessed by a transthoracic echocardiography and nuclear medicine scintigraphy, but depended on factors associated with volume overload. The authors emphasize that, because bioimpedance results might be affected by malnutrition with a loss of cell mass, NT-proBNP levels may be elevated in people with malnutrition.[22]

Although nutritional status is assessed by BMI in everyday practice, this index does not distinguish between fat and lean body mass. In their PLICA study, Gastelurrutia et al[42] focused on the muscle wasting that accompanies CHF and concluded that nutritional status is a key prognostic factor above and beyond BMI and percentage of body fat. Patients in normal, overweight, and obese BMI ranges all experienced undernourishment. The high mortality observed in undernourishment, uncommon in patients with high BMI,

TABLE 4 Logistic regression model for the risk of malnutrition (Mini Nutritional Assessment score <24) in patients with chronic heart failure (n = 76)

Characteristics		OR	95% CI	*P* value
NT-proBNP	1st	1.00	Ref.	–
	2nd	5.05	0.39–65.2	0.22
	3rd	26.2	2.12–324.28	0.01
Age		1.01	0.96–1.07	0.68
Chronic kidney disease (yes vs no)		1.29	0.35–1.71	0.70
IADL		0.99	0.85–1.16	0.95
MMSE		0.78	0.63–0.95	0.02
No. of diseases[a]		1.32	0.77–2.24	0.31

a Chronic heart failure, coronary heart disease, myocardial infarction, stroke, valvular heart disease, diabetes, or arthritis

Abbreviations: see TABLES 1 and 2

may help explain the obesity paradox.[42] There is no universal standard for a nutritional assessment, and HF, a chronic disease associated with body wasting and water retention, may require specific considerations. In a pilot study, Gastelurrutia et al[6] demonstrated that a more accurate measurement of nutritional status in patients with HF actually revealed undernourishment among those in normal and high BMI categories; being undernourished was found to be prognostically meaningful.[46]

In our study, we decided to use the MNA, a simple, noninvasive, and well-validated screening tool recommended for early detection of malnutrition risk.[31] To our knowledge, only one study[30] evaluated the association between NT-proBNP and nutritional status using the MNA: a short (MNA-SF) and a full form (MNA-F). Similarly to our results concerning the higher risk of malnutrition with increased NT-proBNP levels, Sargento et al[30] found an inverse correlation between the MNA-SF score and NT-proBNP level ($r = -0.49$; $P < 0.001$) when analyzed as continuous variables. They also showed a strong correlation between both forms ($r = 0.692$, $P < 0.001$). The authors concluded that the MNA is not only useful for the evaluation of nutritional status of elderly outpatients with systolic HF and a good predictor of short-term outcome, but it is also associated with quality of life and NT-proBNP.[30] However, they analyzed patients with systolic HF, while the type of HF was not distinguished in our analysis.

Our study has a few limitations. A considerable limitation is the cross-sectional design, which may be associated with unmeasured confounders. Also, our study group was rather small, which limits the number of covariates used in the model and limits division participants into subgroups (eg, according to the MNA score or according to sex). The increase in NT-proBNP level is age-related and women, in general, have a higher NT-proBNP concentration in comparison with men[47]; however, because of our small sample size, men and women were not assessed separately. Another limitation is the fact that we defined CHF by clinical symptoms and an ejection fraction; we did not assess diastolic function of the heart. Therefore, higher NT-proBNP levels in patients without diagnosis or symptoms of HF may be due to long-term hypertension, medications, or compensated CHF. In the latter, the patient would be asymptomatic despite increased plasma BNP and NT-proBNP concentrations.

Finally, the number of patients in the groups with and without HF was uneven, with fewer participants in the group without defined HF.

In conclusion, high NT-proBNP levels contribute to increased risk of malnutrition in elderly patients with HF. Elderly patients with elevated NT-proBNP levels should be assessed for the risk of malnutrition. However, to confirm these findings and gain a more in-depth understanding of this issue, further research is needed to investigate the associated mechanisms, the relationship between fat mass and lean body mass, the obesity paradox in elderly individuals with HF, and the possibility of improving HF treatment to reduce the risk of malnutrition. In addition, the potential role of NT-proBNP as a good predictor of malnutrition risk assessed by the MNA needs to be explored.

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CONTRIBUTION STATEMENT AS conceived the concept of the study. PF, AS, and MF-Ł contributed to the design of the research. All authors were involved in data collection. AP performed the statistical analysis. MF-Ł coordinated funding for the project. All authors edited and approved the final version of the manuscript.

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